Appln No.: 09/719,494
Amendment Dated: July 29, 2004
Reply to Office Action of March 31, 2004

REMARKS/ARGUMENTS

This is in response to the Office Action mailed March 31, 2004 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants request an extension of time to make this paper timely and enclose the fee. The Commissioner is authorized to charge any additional fees or credit any overpayment to Deposit Account No. 15-0610.

Non-elected claims 17-33 have been canceled, without prejudice.

Claim 1 has been amended to refer only to non-immunogenic target peptides, and not to include the alternative of weakly immunogenic target peptides as previoulsy set forth.

Claims 1, 2, 9, 11 and 12 are rejected as anticipated by WO 95/29193, relying on extrinsic evidence from Overwijk et al. This evidence establishes that gp100 is, in the Examiner's words, "poorly immunogenic." It is not, however, non-immunogenic. Accordingly, this rejection should be withdrawn.

The Examiner also rejected claims 1, 2 and 9 under 35 USC § 102 as anticipated by Lipford. In this case, the Examiner relies on a teaching of changing of a peptide from one which is non-immunogenic to one which is immunogenic, but does not address whether HPV antigen E6 is itself a target peptide within the scope of the present claims, i.e., one which is non-immunogenic under the circumsatnces set forth in the claim. The Examiner has stated that the claims do not recite whether the target antigen is non-immunogenic but only the target peptide. Applicants respectfully point out that the claims require the target peptide to be one that is expressed by tumor cells of the mammalian subject. Nothing about Lipford suggests that the artificial peptide described is itself expressed in the tumor, or that the actual peptide expressed lacks immungenicity. Indded, since E6 is a viral protein and foreign to a subject mammal, it is expected to be immunogenic. Accordingly, the rejection for anticipation should be withdrawn.

The Examiner rejected claim 2 as anticipated by Dyall et al. Applicants now enclose a *Katz* declaration (three copies, signed in counterparts) which removes the paper as art, because it is not the work of another, and therefore could not have been published before the present invention was made. Accordingly, this rejection should be withdrawn.

The Examiner rejected claims 1, 2, 9 and 16 as anticipated by Huard et al. "as evidenced by admission in the instant specification on page 13, lines 20-23." Without admitting that the Huard reference is in fact prior art, and reserving the right to submit a declaration antedating the document, Applicants point out that Huard does not teach anything about the induction of a

cellular immune response to a target peptide that is expressed in tumor cells of the subject, and that is non-immunogenic when expressed. Thus, there is no anticipation and the rejection should be withdrawn.

Claims 2, and 4 are rejected under 35 USC § 103 as obvious over Dyall in view of Anderson and Yewdell. This rejection is overcome by the declaration to be showing that the Dyall reference is not prior art.

Claims 1-4, 7-9, 11 and 12 are rejected as obvious over WO 95/29193 in view of Anderson or Yewdell. The deficiency of WO 95/29193 because gp100 is not a target peptide within the scope of the present claims has been discussed above. Anderson and Yewdell do not relate to this aspect of the claims. Accordingly, they do nothing to add or suggest the feature which is missing from WO 95/29193. The same is true of the rejection of claims 1-4, 7-9 and 11 over the combination of Lipford, Anderson and Yewdell. Furthermore, Applicants would like to point out that the present invention represents the very antithesis of obviousness. It is known in the art that peptides (such as gp100) which *in vitro* appear to generate good immune responses do not make good targets for immunization purposes because no real and effective immune response is generated. The present invention relies on the paradoxical effect observed by the present inventors and not suggested in the art that a molecule that produces no immune response in the first instance actually can give rise to an effective vaccine. Thus, these rejections for obviousness should be withdrawn.

The Examiner rejected claims 1, 2, 9 and 16 as obvious over Huard et al. and claims 1-4, 7-9 and 16 as obvious over Huard et al in view of Anderson and Yewdell. Without admitting that the Huard reference is in fact prior art, and reserving the right to submit a declaration antedating the document, Applicants again point out that Huard does not teach anything about the induction of a cellular immune response to a target peptide that is expressed in tumor cells but is non-immunogenic when so expressed. Further, the examiner has not set forth any reason why one would expect the actual target peptide (not a selected portion thereof) to be non-immunogenic, or why a person skilled in the art would find it obvious that an immune response to an inherently non-immunogenic target could be useful in this way to generate an immune response to the target.

It should be noted that the issue in this case is not whether one can take a non-immunogenic peptide and make substitutions that make it immunogenic. The more significant issue is whether one can take a peptide (including a protein) molecule expressed in a tumor cell that is inherently non-immunogenic, and by modifying a selected portion of that sequence create a therapeutic peptide that induces an effective immune response against the original, non-immunogenic target. Nothing in the art suggests that this is the case.

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In view of the foregoing, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,

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